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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/804,457	03/12/2001	Michael P. Maher	AUROBIO.026A	8759

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EXAMINER	
PAK, MICHAEL D	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 05/16/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/804,457	MAHER ET AL.	
	Examiner	Art Unit	
	Michael Pak	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,10-29,49 and 50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8, 10-29, 49 and 50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4-19-04, 8-25-05,* 3-9-06
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. The claims and response filed 28 October 2005 has been entered.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Applicant's arguments filed 28 October 2005, have been fully considered but they are not found persuasive.

Claim Rejections - 35 USC § 103

4. Claims 1-8, 10-29, 49 and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gonzalez et al. (1995) in view of Reiner et al. (1995).

The reason for the rejection has been set forth previously.

Gonzalez et al. teaches a method for achieving fast ratiometric voltage-sensitive fluorescence changes in single cells using fluorescence resonance energy transfer. The mechanism is based on hydrophobic fluorescent anions that rapidly redistribute from one face of the plasma membrane to the other according to the Nernst equation (Gonzalez, page 1272). In this method L-M(TK-) fibroblasts were loaded with DIBAC(3), a fluorescent dye to monitor membrane potential transients, and coated with fluorescein-labeled wheat germ agglutinin (Ibid, page 1273), this pair serves as the fonor-acceptor pair for the energy transfer. The L-M(TK-) cells have low background

currents (Ibid, page 1275). The method teaches the measurement of fluorescent changes of the DISBAC(3) in response to voltage changes (Ibid, page 1276, figure 4). The change in the transmembrane potential is measured without the use of the patch clamp technique. In this Figure, the voltage steps are applied with the patch clamp technique, while the output is measured by monitoring the fluorescence. The electric field would not vary over the area of observation, which in this case is a single cell. Gonzalez further teaches monitoring the fluorescence intensity changes, indicative of membrane potential, in response to square wave step depolarizations from the –70mV holding potential to 40, 80, 120 and 160 mV (Ibid, page 1277, Figure 6). Again, the voltage steps are applied with the patch clamp technique, while the indicia of membrane potential is the fluorescence intensity. The step potentials are applied for 500 milliseconds. Gonzalez et al. further teaches the practice of this method in neonatal cardiac myocytes, which comprise voltage gated ion channels, which are activated upon depolarization (Ibid, page 1278, figure 8). Gonzalez et al. does not teach characterizing the effect of a compound on ion channel activity of a compound with this method.

Renier et al. teaches a method to evaluate expression of functional CFTR. The technique uses the potential-sensitive probe DISBAC2(3), by single-cell fluorescence imaging. The DISBAC(3) method was first validated on the mouse mammary tumor cell line C127, stably expressing wild-type CFTR (Renier, page 1278, Figure 1). Activation of protein kinase A by the cAMP-permeable analogue 8-Br-cAMP induced cell membrane depolarization consistent with expression of wild-type CFTR. The effect of 8-Br-cAMP on A549 cells transfected with adenovirus encoding CFTR was then

measured (Ibid, page 1279, Figure 2). Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to practice a method of characterizing the effect of a compound on ion channel function by exposing a cell expressing the ion channel to alterations in the electric field and measuring the effect on the membrane potential with fluorescent dyes. The motivation is provided in the Renier reference which teaches that the DISBAC(3) method is quick, simple, and reproducible, and does not require invasive cell loading procedures (Ibid, page 1275). The expectation of success is provided in the Gonzalez reference which teaches that voltage indicators based on FRET may already be practically useful and that modest, rationally attainable improvements in sensitivity and speed could make them superior for many biological applications.

5. No claims allowed.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Pak, whose telephone number is (571) 272-0879. The examiner can normally be reached on Monday through Friday from 8:30 AM to 2:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on (571) 272-0835.

The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or

Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michael Pak
Primary Patent Examiner
Art Unit 1646
13 May 2006